

## A Clinical Evaluation of Thrombo-Wellcotest as A Screening Test for D.I.C.

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Many screening tests have been developed for the detection of FDP for the last decade. Of these, Thrombo-Wellcotest was chosen in our laboratory as a screening procedure.

For the last one year, there were 121 determinations performed on 82 patients.

Of the patients suspected to have DIC, 27 patients with clinical, and laboratory evidence of DIC showed the Thrombo-Wellcotest to be positive with titers ranging from 1:5 to 1:1280. Those patients without clinical or laboratory evidence of DIC gave all negative results except for 7 positives with low titers.

It is our opinion that the Thrombo-Wellcotest is a simple procedure to be performed by ordinary laboratory personnel and an inexpensive test which can be afforded by most of the patients. As a whole, the Thrombo-Wellcotest is considered to be a useful screening test for the detection of FDP in serum.

The rapid detection and accurate quantification of fibrinogen/fibrin degradation products (FDP) in serum has assumed major importance in the diagnosis and management of disseminated intravascular coagulation (Colman *et al.* 1972). Of several methods measuring FDP (Erickson *et al.* 1972), a new latex agglutination test, the Thrombo-Wellcotest has recently become commercially available and been widely used. The test is relatively inexpensive and all reagents are supplied in kit form by the manufacturer.

By testing of serum sample at serial dilutions, the approximate concentration of FDP can also be determined.

In our laboratory, we set up the test in 19

78 and evaluation was made after a period of one year.

### MATERIALS AND METHODS

One hundred and twenty-one FDP determinations were performed on 82 suspected cases of DIC who came to Severance Hospital for evaluation over a period of one year.

FDP levels were measured by the Thrombo-Wellcotest supplied by Wellcome Research Laboratories, England.

Thrombo-Wellcotest is a latex agglutination test coated specifically with antibody to purified fibrinogen degradation products and capable of detecting the presence of all the major breakdown products of fibrin or fibrinogen.

Sample tubes contain thrombin to promote complete clotting and enzyme inhibitor to

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prevent secondary fibrinolysis in vitro.

The sensitivity of the reagents is adjusted so that, in the presence of fibrinogen concentrations of 2 ug/ml or greater, the latex particles clump together giving macroscopic agglutination. So the positive 1:5 titer implies the presence of more than 10 ug/ml of FDP and thus far exceeds the normal range determined by the most sensitive method.

In the diagnosis of DIC, we use the criteria for DIC proposed by Branson and Scher., (1976) as seen in Table 1. They proposed hemorrhagic diathesis, hypotension or shock, and oliguria or anuria as clinical criteria and a fibrinogen level below 175 mg/dl, platelet count below 150000/mm<sup>3</sup>, a prothrombin time 7 seconds more than control, an activated partial thromboplastin time 7 seconds more than control, and thrombin time 7 seconds more than control as laboratory criteria.

The 27 patients having one or more clinical, and two or more laboratory criteria were considered to have DIC and correlated with the results of the Thrombo-Wellcotest.

**RESULTS**

The Thrombo-Wellcotest was positive in

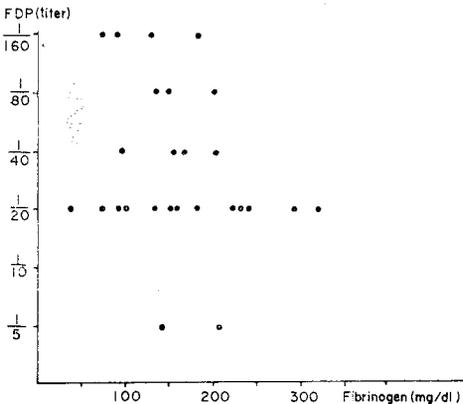


Fig. 1. Correlation between FDP titers and fibrinogen levels in patients with DIC.

all DIC patients, ranging from a titer of 1:5 to 1:1230. Only two failed to have a titer of 1:20 or greater. Of the 25 patients with titers of 1:20 or greater, all appeared to have DIC. The most common underlying condition of DIC in our series was septicemia and the remaining cases had obstetrical disease, leukemia, malignancy, or Korean epidemic hemorrhagic fever (Table 3).

Seven patients without clinical or laboratory evidence of DIC showed positive titers. All of them had titers of 1:5 and no one turned out to have a titer of 1:20 or greater. Three of them were cases with pneumonia, two with liver cirrhosis, one with osteomyelitis, and

Table 1. Criteria for DIC

A. Clinical Criteria	
1. Hemorrhagic diathesis	
2. Hypotension or shock	
3. Oliguria or anuria	
B. Laboratory Criteria	
1. Fibrinogen	≤175 mg/dl
2. Platelet count	≤150,000/cu mm
3. Prothrombin time	7 seconds more than control
4. Partial thromboplastin time	7 seconds more than control
5. Thrombin time	7 seconds more than control

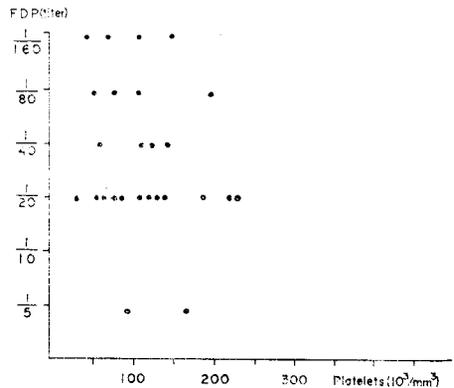


Fig. 2. Correlation between FDP titers and platelets in patients with DIC.

**Table 2. Positive titers in patients without other evidences of DIC**

Titer	No. of patients	Conditions
1:5	7	Osteomyelitis Pneumonia Liver cirrhosis
1:20 or more	0	None

**Table 3. Classification of DIC patients according to Thrombo-Wellcotest titer**

Titer	No. of patients	Conditions
1:5	2	ITP Hemolytic anemia
1:20	13	Septicemia AML ALL IUPD E.H. fever
1:40	5	Septicemia Malignancy Abruptio placenta
1:80	3	Septicemia SLE Typhoid fever
1:160 or more	4	Septicemia E.H. fever SBE
Total	27	

one with erysipelas (Table 2).

The two important parameters of DIC, fibrinogen level and platelet count were correlated with FDP titer. Nearly half of DIC patients, whether they had high or low titers of FDP, revealed normal or slightly elevated fibrinogen levels (Fig. 1). Most patients with DIC, especially with high titers of FDP, revealed low platelet count (Fig. 2).

## DISCUSSION

The recognition and serial measurement of abnormal elevations of FDP levels serve as an index of the degree and clinical progression of fibrinolysis following DIC.

Several methods are available for measuring FDP. To date, the most sensitive quantitative assay of FDP has been the tanned red cell erythrocyte hemagglutination-inhibition test (TRCHII) (Marder *et al.*, 1971). However, the TRCHII is time consuming and technically difficult. Another described test for quantitation of FDP, the staphylococcal clumping test, is as sensitive and reliable as TRCHII, but also requires specialized laboratory preparation and standardization.

Agglutination of latex particles sensitized with antifibrinogen antibody has provided a simple rapid method for the detection of FDP. However, the formerly available Fi-test (Hyl- and Laboratories, Los Angeles, California) had led to a high incidence of false negative results (Thomas *et al.*, 1970).

A new latex agglutination test, the Thrombo-Wellcotest, coated specifically with antibody to FDP D and E as well as X and Y has recently become commercially available and been widely used in clinical or research laboratories (Ellman *et al.*, 1973).

Garvey and Black (1972) compared the Thrombo-Wellcotest with TRCHII and reported a similar, excellent correlation between the two tests in a variety of diseases.

Carvalho *et al.* (1976) also compared the Thrombo-Wellcotest with the staphylococcal clumping test and reported a significant and excellent correlation between the two tests.

In our study, of the 27 patients with DIC according to the criteria of Branson and Schmer (1976), only two failed to have a titer of 1:20 or greater.

On the basis of our experience, it appears that the Thrombo-Wellcotest is inexpensive, simple enough to be performed by ordinary laboratory personnel, and useful for the screening of DIC.

One third of patients with DIC in this study showed a normal range of fibrinogen concentration in their plasma. Similarly, platelet counts were above  $150 \times 10^3/\text{mm}^3$  in 5 cases among 27 DIC cases. These cases seem to have been compensated by the liver and bone marrow.

The liver is capable of generating considerably more fibrinogen than it does normally, and the marrow can produce up to 10 times the normal of platelets (Harker and Finch, 1969).

Therefore it seems reasonable to believe that the actual concentration of fibrinogen in the plasma and the number of platelets in the blood reflect the balance between rates of synthesis and rates of destruction. In other words, the manifestations of DIC syndrome depend on the degree of compensation afforded by the liver or the marrow, and these may not be the same for the two organs. Thus, hyperfibrinogenemia and thrombocytopenia could coexist and represent a more effective compensation to the DIC syndrome (Cooper *et al.*, 1974).

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